Oxidative Coupling of Benzo-4H-pyran-4-ones and Benzene by Palladium (II) Acetate

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Abstract

The oxidation of benzo-4H-pyran-4-ones by palladium (II) acetate in acetic acid containg benzene gave the corresponding flavone derivatives, accompanied by biphenyl.

Introduction

Aryl-substituted aromatic heterocycles are interesting compounds as precursors to biologically and physiologically active compounds and also in connection with the existence of naturally occurring compounds such as flavones (**1**) and isoflavones (**2**). Oxidative coupling between aromatic heterocycles and arenes in an efficient and simple method for the preparation of the aryl-substituted aromatic heterocycles. However, no report of oxidative cross-coupling between aromatic heterocycles except furans,[1,2] thiophenes,[1] pyrroles,[1] indoles[1] and isoxazoles [3]and arenes by palladium (II) acetate has been published. The present paper deals with the oxidative coupling between benzo-4H-pyran-4-ones(**3**) and benzene by palladium (II) acetate.

Results and Discussion

Usually the compounds **1** and **2** have been prepared by ring-synthesis. However, no report of direct arylation of **3** to give **1** or **2**. We have now found that treatment of **3** with benzene and palladium (II) acetate led to the arylation on C-2 of **3** and gave the corresponding **1** together with biphenyl(**4**).

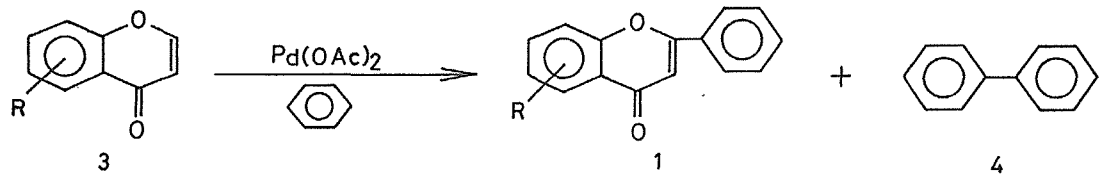
For example, oxidation of benzo-4H-pyran-4one (**3a**) by palladium (II) acetate in acetic acid which contained benzene at reflux temperature gave a mixture of flavone (**1a**) and **4** but none of isoflavone (**2a**). Under similar conditions, treatment of 6-methylbenzo-4H-pyran-4-one (**3b**), 7-methylbenzo-4H-pyran-4-one (**3c**), 8-methylbenzo-4H-pyran-4-one (**3d**) and 7-methoxybenzo-4H-pyran-4-one (**3e**) with palladium (II) acetate in a mixture of acetic acid and benzene gave 6-methylflavone(**1b**), 7-methylflavone(**1c**), 8-methylflavone(**1d**), and 7-methoxyflavone (**1e**) respectively, accompanied by **4**. These results are summarized in Table 1.

Generally it is known that reaction at the C-2 position of benzo-4H-pyran-4-one ring is not easy. For example, the bromination of **3a** with bromine led to the formation of 3-bromobenzo-4H-pyran-4-one[4], and the Mannich reaction of **3** with dimethylamine afforded 3-dimethylaminomethylbenzo-4H-pyran-4-one[5]. The arylation of **3** with

Table 1. Phenylation of Benzo-4H-pyran-4-one **3** with Palladium (II) Acetate and Benzene.

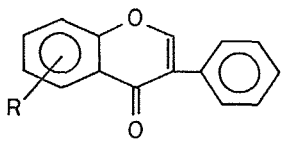
Substrate	Products	(isolated yields,[a] %)		
3a	1a	(18);	4	(39)
3b	1b	(22);	4	(43)
3c	1c	(16);	4	(35)
3d	1d	(24);	4	(32)
3e	1e	(16);	4	(42)

a) Yields based on palladium acetate used.



3 1 4

1a , 3a : R = H
1b , 3b : R = 6-CH_3
1c , 3c : R = 7-CH_3
1d , 3d : R = 8-CH_3
1e , 3e : R = 7-OCH_3



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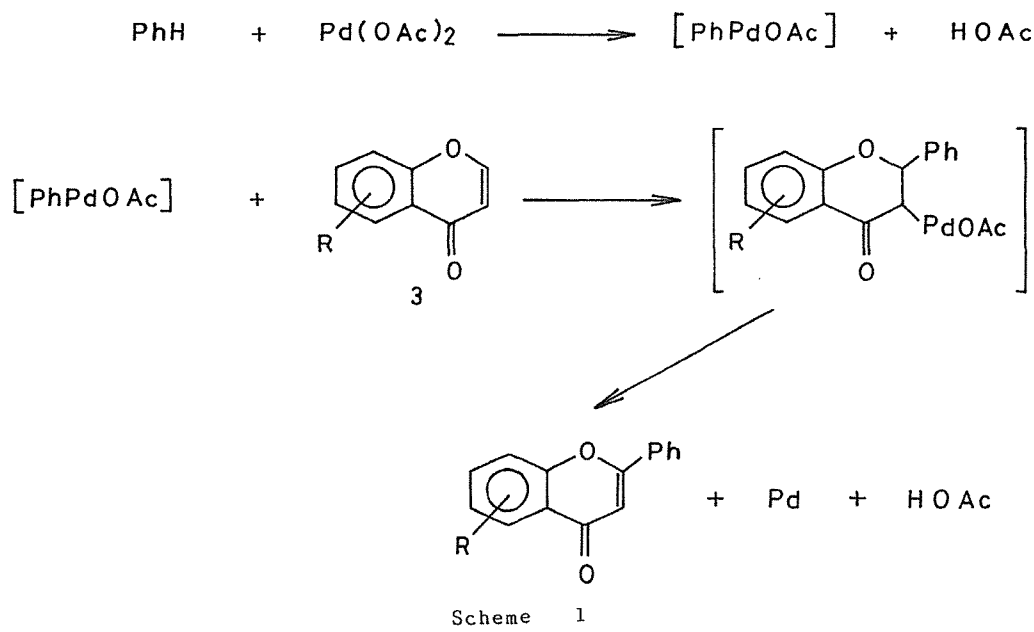
palladium(II) acetate and benzene is, therefore, of interest as an unusual substitution at the C-2 position of benzo-4H-pyran-4-one ring. In view of the known reports on the oxidative coupling of arenes and aromatic heterocycles[6] and our present results, it seemed reasonable to assume that the coupling of **3** and benzene proceeded via aryl- or heteroaryl-palladium (II) intermediates, as shown in Scheme 1.

Coupling reaction of olefins and aromatic heterocycles such as furans, thiophenes, and indoles, are an effective method for the preparation of important precursors of biologically and physiologically active compounds, However, the oxidative coupling of **3** and olefins such as styrene or ethyl acrylate by palladium(II)acetate did not give the expected coupling products, and gave the dimerization products of olefins.

Experimental

Melting points were determined with a Gallenkamp melting point apparatus and are uncorrected.



Scheme 1

Benzo-4H-pyran-4-one (**3a**)[7], 6-methylbenzo-4H-pyran-4-one (**3b**)[4], 7-methylbenzo-4H-pyran-4-one(**3c**)[4], 8-methylbenzo-4H-pyran-4-one (**3d**)[4], and 7-methoxybenzo-4H-pyran-4-one(**3e**)[8] were prepared according to the procedure described in literatures.

General Procedure for the Reaction of Benzo-4H-pyran-4-one (**3**) *with Benzene and Palladium (II) Acetate.*

A solution of **3** (4.46mmol)and palladium (II) acetate (1.00g, 4.46mmol) in a mixture of acetic acid (110 ml) and benzene (110ml) was heated at 80℃ with stirring under nitrogen. After 14 h, the reaction mixture was evaporated to give a residue which was then column-chromatographed by sillica gel using benzene as eluent to give **1** and **4**. These results are summarized in Table 1. The spectral data and analytical data of the products are given below.

Flavone (**1a**): colorless crystals, mp97-98℃ (lit.[9] mp96-98℃); Ir(potassium bromide): 1640 (C=O), 1620 (C=C), 765, 755, 680cm^{-1} (aromatic ring); ^{1}H-nmr(deuteriochloroform/TMS) δ 6.82 (C_3-H), 7.24-8.28pp (m, 9H, aromatic protons).

6-Methylflavone(**1b**): colorless crystals, mp87-88℃ (lit.[10] mp120-121℃): Ir (potassium bromide): 1640 (C=O), 1620 (C=C), 870, 820, 750, 690cm^{-1} (aromatic ring); ^{1}H-nmr (deuteriochloroforms/TMS): δ 2.27 (s, 3H, CH_3), 6.78 (s, 1H, C_3-H), 6.90-8.04ppm (m, 8H, aromatic protors).

7-Methylflavone(**1c**): colorless crystals, mp119-120℃ (lit.[11] mp120℃), Ir (potassium bromide): 1645 (C=O), 860, 815, 750, 690cm^{-1} (aromatic ring); ^{1}H-nmr (deuteriochloroforms/TMS): δ 2.26 (s, 3H, CH_3), 6.80 (s, 1H, C_3-H), 7.18-8.12 ppm (m, 8H, aromatic protons).

8-Methylflavone(**1d**): colorless crystals, mp168-169℃ (lit.[10] mp170℃), Ir (potassium bromide): 1635 (C=O), 1620 (C=C), 770, 750, 690cm^{-1} (aromatic ring); ^{1}H-nmr (deuteriochloroforms/TMS): δ 2.52(s, 3H, CH_3), 6.75(s, 1H, C_3-H), 7.08-8.10ppm (m, 8H, aomatic protons).

7-Methoxyflavone (**1e**): pale yellow crystals, mp108-109℃ (lit.[12] mp109-110℃); Ir

(potassium bromide) : 1650 (C=O), 1620 (C=C),900, 815, 765, 680cm^{-1}(aromatic ring); ^{1}H-nmr (deuteriochloroform/TMS) :δ 3.90 (s, 3H,OC$\underline{H}_3$),6.72(s, 1 H, C_3-$\underline{H}$),6.90-8.06ppm(m, 8 H, aromatic protons).

Biphemyl (4) : mp68-69℃ (lit.[13] mp 69-70℃) .

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